AMENDMENTS TO THE CLAIMS

1. (cancelled)

2. (currently amended) A method of claim 19 ~~the compound of claim 1~~ wherein $Z^1$ and $Z^2$ are each $R^7$-aryl.

3. (currently amended) A ~~compound~~ method of claim 2 wherein $Z^1$ and $Z^2$ are each $R^7$-phenyl.

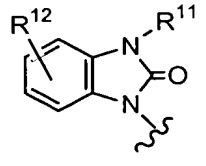
4. (currently amended) A ~~compound~~ method of claim 3 wherein $R^7$ is selected from the group consisting of $(C_1$-$C_6)$alkyl and halo.

5. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein $R^1$, $R^2$, $R^3$ and $R^4$ are each hydrogen.

6. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein $R^1$ and $R^3$ are each hydrogen and $R^2$ and $R^4$ are an alkylene bridge of 2 or 3 carbons.

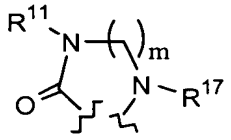
7. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein $X^1$ is $R^7$-aryl and and $X^2$ is OH or [-NC(O)$R^{28}$] –NC(O)$R^{21}$.

8. (currently amended) A method ~~compound~~ of claim 7 wherein $X^1$ is $R^7$-phenyl.

9. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein $X^1$ is  and $X^2$ is hydrogen.

10. (currently amended) A method ~~compound~~ of claim 9 wherein $R^{12}$ is hydrogen and $R^{11}$ is $(C_1\text{-}C_6)$alkyl, -$(C_1\text{-}C_6)$ alkyl$(C_3\text{-}C_{12})$cycloalkyl, -$(C_1\text{-}C_6)$alkyl-$OR^{19}$ or -$(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$.

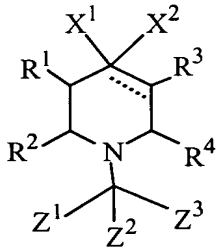
11. (currently amended) A method of claim 19 ~~compound of claim 1~~ wherein $X^1$ and $X^2$ together form the spirocyclic group



12. (currently amended) A method ~~compound~~ of claim 11 wherein m is 1, $R^{17}$ is phenyl and $R^{16}$ is -$(C_1\text{-}C_6)$alkyl-$OR^{19}$ or -$(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$.

13 to 18. (cancelled)

19. (new) A method of treating cough comprising administering a combination of an effective amount of an ORL-1 agonist of the formula



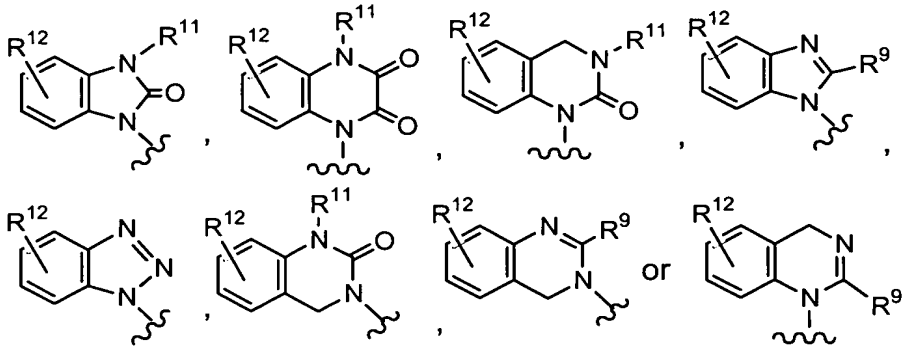
or a pharmaceutically acceptable salt or solvate thereof, wherein:

the dotted line represents an optional double bond;

$X^1$ is $R^5$-$(C_1\text{-}C_{12})$alkyl, $R^6$-$(C_3\text{-}C_{12})$cycloalkyl, $R^7$-aryl, $R^8$-heteroaryl or $R^{10}$-$(C_3\text{-}C_7)$heterocycloalkyl;

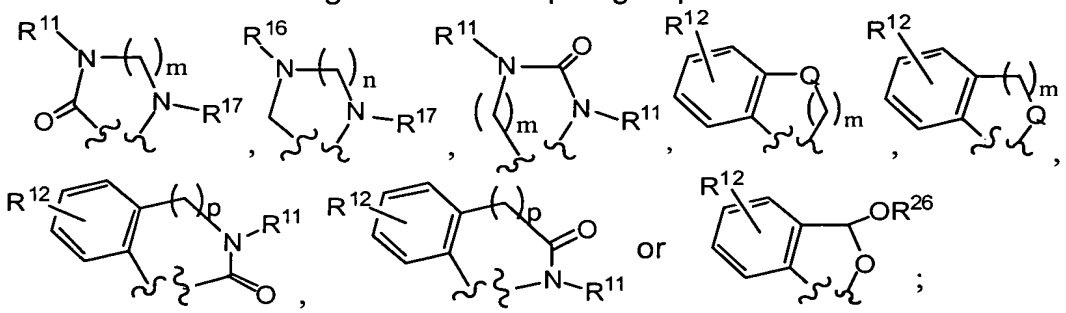
$X^2$ is -CHO, -CN, -$NHC(=NR^{26})NHR^{26}$, -$CH(=NOR^{26})$, -$NHOR^{26}$, $R^7$-aryl, $R^7$-aryl$(C_1\text{-}C_6)$alkyl, $R^7$-aryl$(C_1\text{-}C_6)$alkenyl, $R^7$-aryl$(C_1\text{-}C_6)$-alkynyl, -$(CH_2)_vOR^{13}$, -$(CH_2)_vCOOR^{27}$, -$(CH_2)_vCONR^{14}R^{15}$, -$(CH_2)_vNR^{21}R^{22}$ or -$(CH_2)_vNHC(O)R^{21}$, wherein v is zero, 1, 2 or 3 and wherein q is 1 to 3 and a is 1 or 2;

or $X^1$ is



and $X^2$ is hydrogen;

or $X^1$ and $X^2$ together form a spiro group of the formula



m is 1 or 2;

n is 1, 2 or 3, provided that when n is 1, one of $R^{16}$ and $R^{17}$ is $-C(O)R^{28}$;

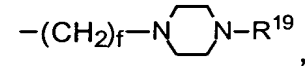
p is 0 or 1;

Q is $-CH_2-$, -O-, -S-, -SO-, $-SO_2-$ or $-NR^{17}-$;

$R^1$, $R^2$, $R^3$ and $R^4$ are independently selected from the group consisting of hydrogen and $(C_1-C_6)$alkyl, or ($R^1$ and $R^4$) or ($R^2$ and $R^3$) or ($R^1$ and $R^3$) or ($R^2$ and $R^4$) together can form an alkylene bridge of 1 to 3 carbon atoms;

$R^5$ is 1 to 3 substituents independently selected from the group consisting of H, $R^7$-aryl, $R^6$-$(C_3-C_{12})$cycloalkyl, $R^8$-heteroaryl, $R^{10}$-$(C_3-C_7)$heterocycloalkyl, $-NR^{19}R^{20}$, $-OR^{13}$ and $-S(O)_{0-2}R^{13}$;

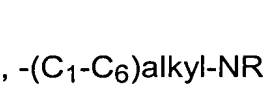
$R^6$ is 1 to 3 substituents independently selected from the group consisting of H, $(C_1-C_6)$alkyl, $R^7$-aryl, $-NR^{19}R^{20}$, $-OR^{13}$ and $-SR^{13}$;

$R^7$ is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, $(C_1\text{-}C_6)$alkyl, $R^{25}$-aryl, $(C_3\text{-}C_{12})$cycloalkyl, -CN, $-CF_3$, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$, $-OCF_3$, $-NR^{19}R^{20}$, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$, $-NHSO_2R^{19}$, $-SO_2N(R^{26})_2$, $-SO_2R^{19}$, $-SOR^{19}$, $-SR^{19}$, $-NO_2$, $-CONR^{19}R^{20}$, $-NR^{20}COR^{19}$, $-COR^{19}$, $-COCF_3$, $-OCOR^{19}$, $-OCO_2R^{19}$, $-COOR^{19}$, $-(C_1\text{-}C_6)$alkyl-$NHCOOC(CH_3)_3$, $-(C_1\text{-}C_6)$alkyl-$NHCOCF_3$, $-(C_1\text{-}C_6)$alkyl-$NHSO_2$-$(C_1\text{-}C_6)$alkyl, $-(C_1\text{-}C_6)$alkyl-NHCONH-$(C_1\text{-}C_6)$-alkyl or  , wherein f is 0 to 6; or $R^7$ substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

$R^8$ is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, $(C_1\text{-}C_6)$alkyl, $R^{25}$-aryl, $(C_3\text{-}C_{12})$cycloalkyl, -CN, $-CF_3$, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$, $-OCF_3$, $-NR^{19}R^{20}$, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$, $-NHSO_2R^{19}$, $-SO_2N(R^{26})_2$, $-NO_2$, $-CONR^{19}R^{20}$, $-NR^{20}COR^{19}$, $-COR^{19}$, $-OCOR^{19}$, $-OCO_2R^{19}$ and $-COOR^{19}$;

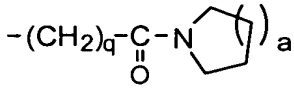
$R^9$ is hydrogen, $(C_1\text{-}C_6)$alkyl, halo, $-OR^{19}$, $-NR^{19}R^{20}$, -NHCN, $-SR^{19}$ or $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

$R^{10}$ is H, $(C_1\text{-}C_6)$alkyl, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$, $-NR^{19}R^{20}$ or $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

$R^{11}$ is independently selected from the group consisting of H, $R^5$-$(C_1\text{-}C_6)$alkyl, $R^6$-$(C_3\text{-}C_{12})$cycloalkyl, $-(C_1\text{-}C_6)$alkyl$(C_3\text{-}C_{12})$cycloalkyl, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$ and  , wherein q and a are as defined above;

$R^{12}$ is H, $(C_1\text{-}C_6)$alkyl, halo, $-NO_2$, $-CF_3$, $-OCF_3$, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$, $-NR^{19}R^{20}$ or $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

$R^{13}$ is H, $(C_1\text{-}C_6)$alkyl, $R^7$-aryl, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$ or $-(C_1\text{-}C_6)$alkyl-$SR^{19}$;

$R^{14}$ and $R^{15}$ are independently selected from the group consisting of H, $R^5$-($C_1$-$C_6$)alkyl, $R^7$-aryl and  , wherein q and a are as defined above;

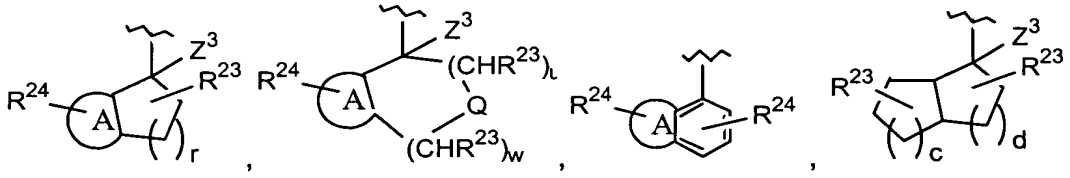
$R^{16}$ and $R^{17}$ are independently selected from the group consisting of hydrogen, $R^5$-($C_1$-$C_6$)alkyl, $R^7$-aryl, ($C_3$-$C_{12}$)cycloalkyl, $R^8$-heteroaryl, $R^8$-heteroaryl($C_1$-$C_6$)alkyl, -C(O)$R^{28}$, -($C_1$-$C_6$)alkyl($C_3$-$C_7$)-heterocycloalkyl, -($C_1$-$C_6$)alkyl-O$R^{19}$ and -($C_1$-$C_6$)alkyl-S$R^{19}$;

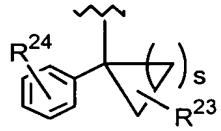
$R^{19}$ and $R^{20}$ are independently selected from the group consisting of hydrogen, ($C_1$-$C_6$)alkyl, ($C_3$-$C_{12}$)cycloalkyl, aryl and aryl($C_1$-$C_6$)alkyl;

$R^{21}$ and $R^{22}$ are independently selected from the group consisting of hydrogen, ($C_1$-$C_6$)alkyl, ($C_3$-$C_{12}$)cycloalkyl, ($C_3$-$C_{12}$)cycloalkyl($C_1$-$C_6$)alkyl, ($C_3$-$C_7$)heterocycloalkyl, -($C_1$-$C_6$)alkyl($C_3$-$C_7$)-heterocycloalkyl, $R^7$-aryl, $R^7$-aryl($C_1$-$C_6$)alkyl, $R^8$-heteroaryl($C_1$-$C_{12}$)alkyl, -($C_1$-$C_6$)alkyl-O$R^{19}$, -($C_1$-$C_6$)alkyl-N$R^{19}R^{20}$, -($C_1$-$C_6$)alkyl-S$R^{19}$, -($C_1$-$C_6$)alkyl-N$R^{18}$-($C_1$-$C_6$)alkyl-O-($C_1$-$C_6$)alkyl and -($C_1$-$C_6$)alkyl-N$R^{18}$-($C_1$-$C_6$)alkyl-N$R^{18}$-($C_1$-$C_6$)alkyl;

$R^{18}$ is hydrogen or ($C_1$-$C_6$)alkyl;

$Z^1$ is $R^5$-($C_1$-$C_{12}$)alkyl, $R^7$-aryl, $R^8$-heteroaryl, $R^6$-($C_3$-$C_{12}$)cyclo-alkyl, $R^{10}$-($C_3$-$C_7$)heterocycloalkyl, -$CO_2$($C_1$-$C_6$)alkyl, CN or -C(O)N$R^{19}R^{20}$; $Z^2$ is hydrogen or $Z^1$; $Z^3$ is hydrogen or ($C_1$-$C_6$)alkyl; or $Z^1$, $Z^2$ and $Z^3$, together with the carbon to which they are attached, form the group



or  , wherein r is 0 to 3; w and u are each 0-3, provided that the sum of w and u is 1-3; c and d are independently 1 or 2; s is 1 to 5; and ring

A is a fused $R^7$-phenyl or $R^8$-heteroaryl ring;

$R^{23}$ is 1 to 3 substituents independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$, $-NR^{19}R^{20}$ and $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

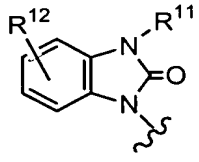
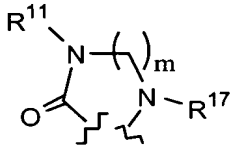
$R^{24}$ is 1 to 3 substituents independently selected from the group consisting of $R^{23}$, $-CF_3$, $-OCF_3$, $NO_2$ or halo, or $R^{24}$ substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

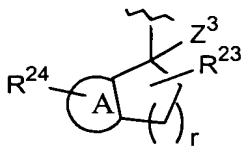
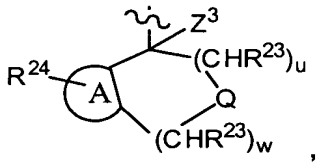
$R^{25}$ is 1-3 substituents independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and halo;

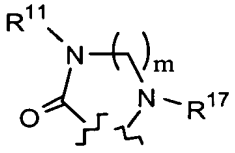
$R^{26}$ is independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl and $R^{25}\text{-}C_6H_4\text{-}CH_2$-;

$R^{27}$ is H, $(C_1\text{-}C_6)$alkyl, $R^7$-aryl$(C_1\text{-}C_6)$alkyl, or $(C_3\text{-}C_{12})$cycloalkyl;

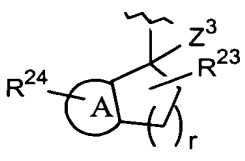
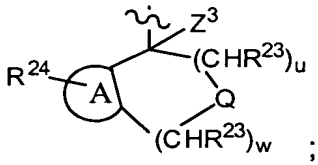
$R^{28}$ is $(C_1\text{-}C_6)$alkyl, $-(C_1\text{-}C_6)$alkyl$(C_3\text{-}C_{12})$cycloalkyl, $R^7$-aryl, $R^7$-aryl-$(C_1\text{-}C_6)$alkyl, $R^8$-heteroaryl, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$ or $-(C_1\text{-}C_6)$alkyl-$SR^{19}$;

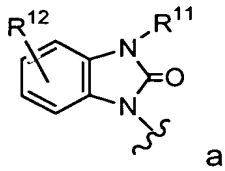
provided that when $X^1$ is  or $X^1$ and $X^2$ together are  and $Z^1$ is $R^7$-phenyl, $Z^2$ is not hydrogen or $(C_1\text{-}C_3)$alkyl;

provided that when $Z^1$, $Z^2$ and $Z^3$, together with the carbon to which they are attached, form  or  , and $X^1$ and $X^2$ together are


, $R^{11}$ is not H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl or $(C_1\text{-}C_6)$hydroxyalkyl;

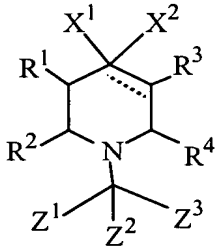
provided that when $R^2$ and $R^4$ form an alkylene bridge, $Z^1$, $Z^2$ and $Z^3$, together with the carbon to which they are attached, are not


or

; and

provided that when $X^1$ is

and $Z^1$ is $R^6$-$(C_3\text{-}C_{12})$-cycloalkyl, $Z^2$ is not H;

and an effective amount of second agent for treating cough, allergy or asthma symptoms selected from the group consisting of: antihistamines, 5-lipoxygenase inhibitors, leukotriene inhibitors, $H_3$ inhibitors, ß-adrenergic receptor agonists, xanthine derivatives, α–adrenergic receptor agonists, mast cell stabilizers, anti-tussives, expectorants, $NK_1$, $NK_2$ and $NK_3$ tachykinin receptor antagonists, and $GABA_B$ agonists.

20. (new) A pharmaceutical composition comprising: a therapeutically effective amount of a nociceptin receptor ORL-1 agonist of the formula



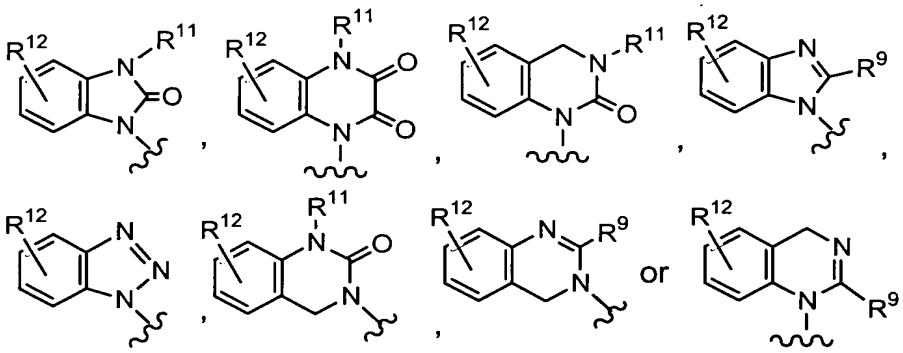
or a pharmaceutically acceptable salt or solvate thereof, wherein:

the dotted line represents an optional double bond;

$X^1$ is $R^5$-($C_1$-$C_{12}$)alkyl, $R^6$-($C_3$-$C_{12}$)cycloalkyl, $R^7$-aryl, $R^8$-heteroaryl or $R^{10}$-($C_3$-$C_7$)heterocycloalkyl;

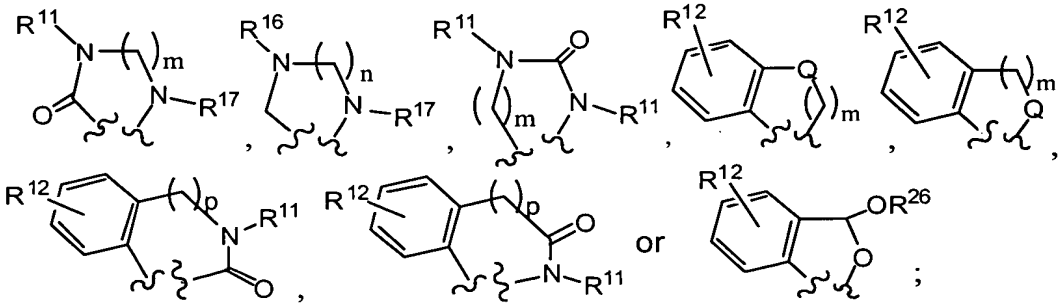
$X^2$ is -CHO, -CN, -NHC(=$NR^{26}$)$NHR^{26}$, -CH(=$NOR^{26}$), -$NHOR^{26}$, $R^7$-aryl, $R^7$-aryl($C_1$-$C_6$)alkyl, $R^7$-aryl($C_1$-$C_6$)alkenyl, $R^7$-aryl($C_1$-$C_6$)-alkynyl, -$(CH_2)_vOR^{13}$, -$(CH_2)_vCOOR^{27}$, -$(CH_2)_vCONR^{14}R^{15}$, -$(CH_2)_vNR^{21}R^{22}$ or -$(CH_2)_vNHC(O)R^{21}$, wherein v is zero, 1, 2 or 3 and wherein q is 1 to 3 and a is 1 or 2;

or $X^1$ is



and $X^2$ is hydrogen;

or $X^1$ and $X^2$ together form a spiro group of the formula



m is 1 or 2;

n is 1, 2 or 3, provided that when n is 1, one of $R^{16}$ and $R^{17}$ is -$C(O)R^{28}$;

p is 0 or 1;

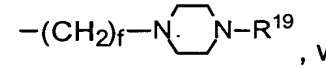
Q is -$CH_2$-, -O-, -S-, -SO-, -$SO_2$- or -$NR^{17}$-;

$R^1$, $R^2$, $R^3$ and $R^4$ are independently selected from the group consisting of hydrogen and ($C_1$-$C_6$)alkyl, or ($R^1$ and $R^4$) or ($R^2$ and $R^3$) or

($R^1$ and $R^3$) or ($R^2$ and $R^4$) together can form an alkylene bridge of 1 to 3 carbon atoms;

$R^5$ is 1 to 3 substituents independently selected from the group consisting of H, $R^7$-aryl, $R^6$-($C_3$-$C_{12}$)cycloalkyl, $R^8$-heteroaryl, $R^{10}$-($C_3$-$C_7$)heterocycloalkyl, -$NR^{19}R^{20}$, -$OR^{13}$ and -$S(O)_{0-2}R^{13}$;

$R^6$ is 1 to 3 substituents independently selected from the group consisting of H, ($C_1$-$C_6$)alkyl, $R^7$-aryl, -$NR^{19}R^{20}$, -$OR^{13}$ and -$SR^{13}$;

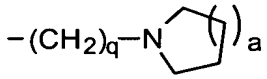
$R^7$ is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, ($C_1$-$C_6$)alkyl, $R^{25}$-aryl, ($C_3$-$C_{12}$)cycloalkyl, -CN, -$CF_3$, -$OR^{19}$, -($C_1$-$C_6$)alkyl-$OR^{19}$, -$OCF_3$, -$NR^{19}R^{20}$, -($C_1$-$C_6$)alkyl-$NR^{19}R^{20}$, -$NHSO_2R^{19}$, -$SO_2N(R^{26})_2$, -$SO_2R^{19}$, -$SOR^{19}$, -$SR^{19}$, -$NO_2$, -$CONR^{19}R^{20}$, -$NR^{20}COR^{19}$, -$COR^{19}$, -$COCF_3$, -$OCOR^{19}$, -$OCO_2R^{19}$, -$COOR^{19}$, -($C_1$-$C_6$)alkyl-$NHCOOC(CH_3)_3$, -($C_1$-$C_6$)alkyl-$NHCOCF_3$, -($C_1$-$C_6$)alkyl-$NHSO_2$-($C_1$-$C_6$)alkyl, -($C_1$-$C_6$)alkyl-NHCONH-($C_1$-$C_6$)-alkyl or  , wherein f is 0 to 6; or $R^7$ substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

$R^8$ is 1 to 3 substituents independently selected from the group consisting of hydrogen, halo, ($C_1$-$C_6$)alkyl, $R^{25}$-aryl, ($C_3$-$C_{12}$)cycloalkyl, -CN, -$CF_3$, -$OR^{19}$, -($C_1$-$C_6$)alkyl-$OR^{19}$, -$OCF_3$, -$NR^{19}R^{20}$, -($C_1$-$C_6$)alkyl-$NR^{19}R^{20}$, -$NHSO_2R^{19}$, -$SO_2N(R^{26})_2$, -$NO_2$, -$CONR^{19}R^{20}$, -$NR^{20}COR^{19}$, -$COR^{19}$, -$OCOR^{19}$, -$OCO_2R^{19}$ and -$COOR^{19}$;

$R^9$ is hydrogen, ($C_1$-$C_6$)alkyl, halo, -$OR^{19}$, -$NR^{19}R^{20}$, -NHCN, -$SR^{19}$ or -($C_1$-$C_6$)alkyl-$NR^{19}R^{20}$;

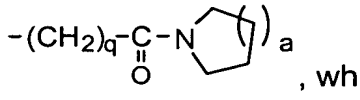
$R^{10}$ is H, ($C_1$-$C_6$)alkyl, -$OR^{19}$, -($C_1$-$C_6$)alkyl-$OR^{19}$, -$NR^{19}R^{20}$ or -($C_1$-$C_6$)alkyl-$NR^{19}R^{20}$;

$R^{11}$ is independently selected from the group consisting of H, $R^5$-($C_1$-$C_6$)alkyl, $R^6$-($C_3$-$C_{12}$)cycloalkyl, -($C_1$-$C_6$)alkyl($C_3$-$C_{12}$)cycloalkyl,

-($C_1$-$C_6$)alkyl-$OR^{19}$, -($C_1$-$C_6$)alkyl-$NR^{19}R^{20}$ and  , wherein q and a are as defined above;

$R^{12}$ is H, ($C_1$-$C_6$)alkyl, halo, -$NO_2$, -$CF_3$, -$OCF_3$, -$OR^{19}$, -($C_1$-$C_6$)alkyl-$OR^{19}$, -$NR^{19}R^{20}$ or -($C_1$-$C_6$)alkyl-$NR^{19}R^{20}$;

$R^{13}$ is H, ($C_1$-$C_6$)alkyl, $R^7$-aryl, -($C_1$-$C_6$)alkyl-$OR^{19}$, -($C_1$-$C_6$)alkyl-$NR^{19}R^{20}$ or -($C_1$-$C_6$)alkyl-$SR^{19}$;

$R^{14}$ and $R^{15}$ are independently selected from the group consisting of H, $R^5$-($C_1$-$C_6$)alkyl, $R^7$-aryl and  , wherein q and a are as defined above;

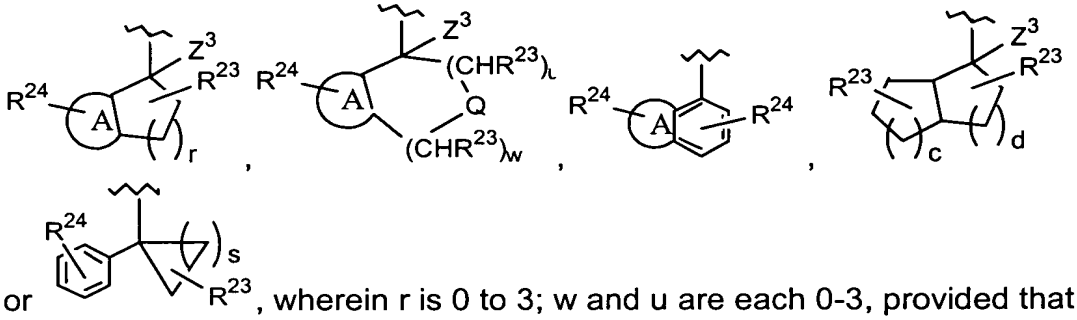
$R^{16}$ and $R^{17}$ are independently selected from the group consisting of hydrogen, $R^5$-($C_1$-$C_6$)alkyl, $R^7$-aryl, ($C_3$-$C_{12}$)cycloalkyl, $R^8$-heteroaryl, $R^8$-heteroaryl($C_1$-$C_6$)alkyl, -C(O)$R^{28}$, -($C_1$-$C_6$)alkyl($C_3$-$C_7$)-heterocycloalkyl, -($C_1$-$C_6$)alkyl-$OR^{19}$ and -($C_1$-$C_6$)alkyl-$SR^{19}$;

$R^{19}$ and $R^{20}$ are independently selected from the group consisting of hydrogen, ($C_1$-$C_6$)alkyl, ($C_3$-$C_{12}$)cycloalkyl, aryl and aryl($C_1$-$C_6$)alkyl;

$R^{21}$ and $R^{22}$ are independently selected from the group consisting of hydrogen, ($C_1$-$C_6$)alkyl, ($C_3$-$C_{12}$)cycloalkyl, ($C_3$-$C_{12}$)cycloalkyl($C_1$-$C_6$)alkyl, ($C_3$-$C_7$)heterocycloalkyl, -($C_1$-$C_6$)alkyl($C_3$-$C_7$)-heterocycloalkyl, $R^7$-aryl, $R^7$-aryl($C_1$-$C_6$)alkyl, $R^8$-heteroaryl($C_1$-$C_{12}$)alkyl, -($C_1$-$C_6$)alkyl-$OR^{19}$, -($C_1$-$C_6$)alkyl-$NR^{19}R^{20}$, -($C_1$-$C_6$)alkyl-$SR^{19}$, -($C_1$-$C_6$)alkyl-$NR^{18}$-($C_1$-$C_6$)alkyl-O-($C_1$-$C_6$)alkyl and -($C_1$-$C_6$)alkyl-$NR^{18}$-($C_1$-$C_6$)alkyl-$NR^{18}$-($C_1$-$C_6$)alkyl;

$R^{18}$ is hydrogen or ($C_1$-$C_6$)alkyl;

$Z^1$ is $R^5$-($C_1$-$C_{12}$)alkyl, $R^7$-aryl, $R^8$-heteroaryl, $R^6$-($C_3$-$C_{12}$)cyclo-alkyl, $R^{10}$-($C_3$-$C_7$)heterocycloalkyl, -$CO_2$($C_1$-$C_6$)alkyl, CN or -C(O)$NR^{19}R^{20}$; $Z^2$ is hydrogen or $Z^1$; $Z^3$ is hydrogen or ($C_1$-$C_6$)alkyl; or $Z^1$, $Z^2$ and $Z^3$, together with the carbon to which they are attached, form the group



or , wherein r is 0 to 3; w and u are each 0-3, provided that the sum of w and u is 1-3; c and d are independently 1 or 2; s is 1 to 5; and ring A is a fused $R^7$-phenyl or $R^8$-heteroaryl ring;

$R^{23}$ is 1 to 3 substituents independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, $-OR^{19}$, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$, $-NR^{19}R^{20}$ and $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$;

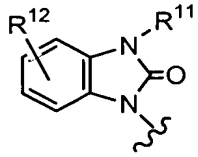
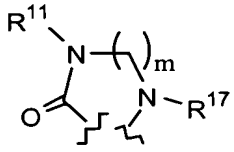
$R^{24}$ is 1 to 3 substituents independently selected from the group consisting of $R^{23}$, $-CF_3$, $-OCF_3$, $NO_2$ or halo, or $R^{24}$ substituents on adjacent ring carbon atoms may together form a methylenedioxy or ethylenedioxy ring;

$R^{25}$ is 1-3 substituents independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy and halo;

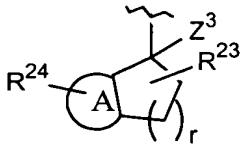
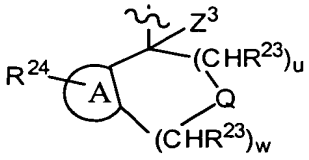
$R^{26}$ is independently selected from the group consisting of H, $(C_1\text{-}C_6)$alkyl and $R^{25}\text{-}C_6H_4\text{-}CH_2$-;

$R^{27}$ is H, $(C_1\text{-}C_6)$alkyl, $R^7$-aryl$(C_1\text{-}C_6)$alkyl, or $(C_3\text{-}C_{12})$cycloalkyl;

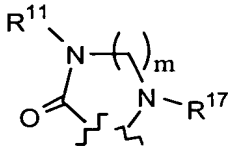
$R^{28}$ is $(C_1\text{-}C_6)$alkyl, $-(C_1\text{-}C_6)$alkyl$(C_3\text{-}C_{12})$cycloalkyl, $R^7$-aryl, $R^7$-aryl-$(C_1\text{-}C_6)$alkyl, $R^8$-heteroaryl, $-(C_1\text{-}C_6)$alkyl-$NR^{19}R^{20}$, $-(C_1\text{-}C_6)$alkyl-$OR^{19}$ or $-(C_1\text{-}C_6)$alkyl-$SR^{19}$;

provided that when $X^1$ is  or $X^1$ and $X^2$ together are  and $Z^1$ is $R^7$-phenyl, $Z^2$ is not hydrogen or $(C_1\text{-}C_3)$alkyl;

provided that when $Z^1$, $Z^2$ and $Z^3$, together with the carbon to which they are attached, form

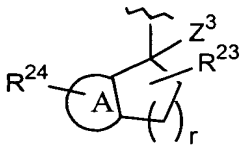
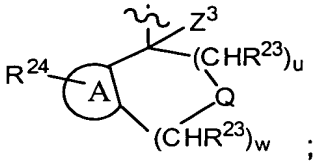



, and $X^1$ and $X^2$ together are

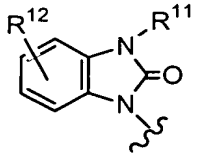


, $R^{11}$ is not H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl or $(C_1\text{-}C_6)$hydroxyalkyl;

provided that when $R^2$ and $R^4$ form an alkylene bridge, $Z^1$, $Z^2$ and $Z^3$, together with the carbon to which they are attached, are not

; and



provided that when $X^1$ is and $Z^1$ is $R^6$-$(C_3\text{-}C_{12})$-cycloalkyl, $Z^2$ is not H; and

a therapeutically effective amount of a second agent selected from the group consisting of: antihistamines, 5-lipoxygenase inhibitors, leukotriene inhibitors, $H_3$ inhibitors, ß-adrenergic receptor agonists, xanthine derivatives, α–adrenergic receptor agonists, mast cell stabilizers, anti-tussives, expectorants, $NK_1$, $NK_2$ and $NK_3$ tachykinin receptor antagonists, and $GABA_B$ agonists; and a pharmaceutically acceptable carrier.